Variability in energy expenditure and its components

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Purpose of review
To review factors contributing to variation in total daily energy expenditure and its primary components: (1) resting metabolic rate; (2) diet-induced thermogenesis; and (3) activity thermogenesis, including exercise energy expenditure and nonexercise activity. For each component, the expected magnitude of intra-individual variability is also considered. We also reviewed studies that quantified the variability in 24 h energy expenditure.

Recent findings
In humans, the coefficient of variation in the components of total daily energy expenditure is around 5–8% for resting metabolic rate, 1–2% for exercise energy expenditure, and around 20% for diet-induced thermogenesis. The coefficient of variance for 24 h energy expenditure measured using a room calorimeter for resting metabolic rate is around 5–10%. Thus, these measures are all rather reproducible. Total daily energy expenditure varies several-fold in humans, not due to variation in resting metabolic rate, diet-induced thermogenesis, or exercise thermogenesis, but rather, due to variations in nonexercise activity. A variety of factors impact nonexercise activity, including occupation, environment, education, genetics, age, gender, and body composition, but little is known about the magnitude of effect.

Summary
Resting metabolic rate, diet-induced thermogenesis, exercise energy expenditure, and 24 h energy expenditure are highly reproducible. Coefficient of variation is smallest for exercise energy expenditure, followed by resting metabolic rate, 24 h energy expenditure, and diet-induced thermogenesis. There is considerable variability in total daily energy expenditure, largely due to variations in nonexercise activity. Although the factors that impact upon nonexercise activity are understood, their contribution to variation in total daily energy expenditure is unclear.

Keywords
diet-induced thermogenesis, exercise thermogenesis, nonexercise thermogenesis, resting metabolic rate, total daily energy expenditure

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Abbreviations

CV	coefficient of variance
DIT	diet-induced thermogenesis
NEAT	nonexercise activity thermogenesis
RMR	resting metabolic rate
TDEE	total daily energy expenditure

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Introduction

Obesity contributes to an increased risk of heart disease, hypertension, diabetes, and some cancers [1,2]. With the prevalence of obesity in adults and children increasing at an alarming rate worldwide [3,4], there is an increased interest in understanding how variations in total daily energy expenditure (TDEE) contribute to overall energy balance. The major energy components of TDEE are resting metabolic rate (RMR), diet-induced thermogenesis (DIT), and activity thermogenesis. RMR is the largest component of TDEE (60–75%), and represents the energy required to maintain essential vital functioning. Three-quarters of the variability in RMR is predicted by lean body mass [5]. DIT is the increase in energy expenditure associated with the digestion, absorption, and storage of food and accounts for approximately 10–15% of TDEE [6]. Activity thermogenesis can be further separated into exercise activity thermogenesis and nonexercise activity thermogenesis (NEAT) components. NEAT includes the energy expenditure of all occupation, leisure, sitting, standing, and ambulation [7].

In order to understand how the components of TDEE contribute to the maintenance of energy balance, it is important to understand the variability of these measurements. Variability in measurements of energy expenditure represents the summed effects of instrument error, investigator error, and of biological variability (within individual, day-to-day variability). The contribution of instrument and investigator error to measures of energy expenditure can be minimized by employing good practices (routine calibration and maintenance of equipment; proper training of laboratory staff). For example, within-machine errors of less than 2% have been reported for two of the most commonly used metabolic measuring systems: the Sensormedics 2900 (Yorba Linda, California) [8] and the Deltatrac MD 1 (Datex, Helsinki, Finland) [8,9], and between-machine errors for the Deltratrac are less than 3% [9].

Many factors contribute to biological variability in energy expenditure, including anxiety (due to unfamiliarity with the testing environment, job and family stresses, etc.), diurnal variation due to circadian rhythms, and recent physical activity and energy intake. These factors must be minimized in order to minimize the contribution of biological variability to overall error. In this review, we summarize findings from studies that have measured the within-subject (intra-individual) variation in energy expenditure and its components. Specifically, we have reviewed the literature pertaining to variability in (1) RMR, (2) DIT, (3) exercise energy expenditure, (4) 24 h energy expenditure measured using room calorimetry, and (5) free-living energy expenditure. We will focus on factors contributing to biological variability, and summarize the expected magnitude of error introduced by these factors. Our goal is to summarize the state of knowledge in this area, while highlighting the most recent findings (past 5 years). The variability in the measurement of substrate oxidation is beyond the scope of our review and will not be discussed.

Resting metabolic rate

Under standard conditions (measured using the ventilated hood technique while the individual is awake and resting in a thermoneutral environment following an 8–12 h fast and at least 12 h abstinence from exercise), the within individual coefficient of variance (CV) in RMR in healthy adult humans is approximately 3–8% when measured on the same [10,11] or different days [12,13••,14]. Although many different indirect calorimeter systems are used in clinical practice, predominantly utilizing the ventilated hood configuration, most of the systems are associated with CVs of around 2–4% [8,9,15].

The CV for RMR in pre-pubertal children (2.6%) [16], pre-pubertal obese girls (5.8%) [17], and in elderly men (3.4–3.6%) and women (2.5–2.6%) [18•] is similar to that reported in healthy adult populations. RMR is elevated in certain disease states, such as cystic fibrosis [19]. The CV in RMR in these patients (4.3%) was also significantly greater than in age and sex-matched controls (2.4%), but similar to the aforementioned studies in healthy adults. Even in healthy adults, however, individual CVs vary from around 0 to 10% [13••], suggesting that large errors in energy requirements are possible when based on a single measurement of RMR.

RMR exhibits a biphasic pattern during the menstrual cycle, with a greater RMR observed in the luteal compared with the follicular phase, presumably due to elevated serum concentrations of estrogen and progesterone [20]. Nonetheless, a recent study by Henry *et al.* [21•] demonstrated that the CV across a single menstrual cycle is similar (mean CV = 4.6 ± 2.2%, range 1.7–10.4%) to that measured in other populations. However, Day *et al.* (personal communication) measured RMR during the early follicular, mid-follicular, and mid-luteal phases (confirmed by estrogen and progesterone concentrations) and found a slightly higher CV (11.1 ± 2.2%, range 8.9–13.3%). The increased CV in the latter study may be due to the fact that the sex hormone environment was different during each phase (low estrogen and progesterone, high estrogen and low progesterone, and high estrogen and progesterone, respectively).

One might expect that RMR measured in outpatient settings will be higher than that measured in inpatient settings. Studies in pre-pubertal girls [17] and adults [22,23], however, have reported no significant differences in RMR or the CV in RMR [22] (W.M. Saris, personal communication) measured under in and outpatient conditions. Individual differences in RMR measured under outpatient conditions would likely be influenced by physical activity in the period preceding the measurement. Adriaens *et al.* [13••], however, recently reported that differences in RMR (CV = 3.3 ± 2.1%) were not explained by differences in nonexercise-related physical activity the day before the measurement. Furthermore, the CV in RMR fell from 5.2 to 3.3% when individuals who did not comply with the 12 h fast were excluded, suggesting that prior food intake, rather than prior physical activity (exclusive of exercise), will have a much greater effect on RMR. In another recent study, Haugen *et al.* [24••] found that RMR measured in the morning under standard testing conditions (CV = 4.5%) was significantly lower (99.0 ± 35.8 kcal/day) compared with an afternoon measurement (CV = 2.8%) obtained under less stringent conditions (4 h fast, no exercise between measurements). Contrary to the findings of the study of Adriaens *et al.* [13••], the change in RMR from morning to afternoon was not related to reporting energy intake after the morning measurement. Nonetheless, these studies indicate that RMR measurements obtained in outpatient settings are highly reproducible, provided there is reasonable control for prior physical activity and food intake.

Diet-induced thermogenesis

The CV for DIT measured with indirect calorimetery is larger than the CV for RMR, typically around 20% [25,26]. In one specific study, Houde-Nadeau *et al.* demonstrated that the within-subject CV for DIT was 10.7% whereas the inter-subject CV for DIT was 24% [27]. Although similar results were obtained with the use of a ventilated hood facemask, or mouthpiece [28], no study has evaluated the potential effect of sampling method on variation in DIT. The timing of measurements (intermittent versus continuous) has been shown to alter both the magnitude and variability of DIT, with intermittent measures giving a 50% lower response but a more replicable measure [26]. DIT is increased when the ambient temperature is decreased from 22 to 16°C

[29]. The duration of measurements also contributes to the variation in DIT, with shorter measurements (<5 h) yielding greater errors [30]. The magnitude of DIT is proportional to the energy content [30] and the protein content [31] of the test meal. Both over and underfeeding on the days prior to measurement have been reported to alter DIT, although the reported effect varies dramatically among the studies (for review, see [32]). Prior activity likely also affects DIT. In one extreme study, Westrate and Hautvast [33] found that the day after a glycogen-depleting exercise, DIT increased by 23%, although this was not significant. The effect of lesser degrees of exercise on DIT has not been systematically evaluated.

The degree to which inter-individual characteristics contribute to variation in DIT is unclear. Lean body mass is a strong determinant of DIT [30]. Weight gain increases and weight loss decreases DIT [34], although some studies have not seen a decrease in DIT with weight loss [25]. Interestingly, it has been reported that DIT falls up to the point when a 10% weight loss has been achieved, but does not change with further weight loss [34]. A reduced DIT has been reported in obese and insulin-resistant individuals [28], although the independent effect of obesity on DIT is controversial [32]. Likewise, age is associated with a decline in DIT in some [35] but not all studies [36]. A lower DIT has been reported in trained individuals [37], but another study reported a positive correlation between DIT and maximum oxygen consumption [38]. It does not appear as though DIT varies over the menstrual cycle [39]. Most recently, genetic factors such as variations in the β_3-adrenoceptor [40•] have been shown to alter DIT. Variations in intestinal fatty acid binding proteins contribute to variations in fat absorption and oxidation and thus might also contribute to variations in DIT [41,42].

Exercise energy expenditure

Few studies have considered the intra-individual variation in energy expenditure during exercise, but two studies by Pereira and colleagues reported CVs of 1.5% (range 0.71–1.86%) in highly trained individuals [43] and 2% (range 0.85–3.28%) in moderately trained individuals [44]. Thus, the available evidence suggests that the variance in exercise energy expenditure is lower during exercise compared with during an RMR measurement. A potential source of variation in exercise energy expenditure is the variation in mechanical efficiency, which has been shown to be higher in children compared with adults [45] and lower in obese compared with lean individuals [46]. Work efficiency increases with weight loss and decreases with weight gain [47•]. Additionally, efficiency is associated with polymorphisms in uncoupling protein 2 [48]. However, the contribution of intra-individual variation in mechanical efficiency to the variation in exercise energy expenditure has not been studied.

Physical activity energy expenditure

Studies have consistently shown a decline in physical activity with aging in men and women [49–51] and this occurs throughout biology. Overall, adult men and women in the US report similar levels of total physical activity, although women are becoming more active [51]. In other countries, such as Canada, England and Australia, men report being 1.5–3 times more active than women [52,53]. In children, there are consistent gender differences, with boys being more active than girls [54,55]. Gender may influence physical activity in more subtle ways. For example, society and culture may dictate that women work both in the public domain and in the home. Where this occurs in agricultural communities, women's energy needs were found to be 30% greater than predicted [56].

There is a substantial amount of data to suggest that overweight individuals show lower activity levels than their lean counterparts [57,58]. This appears to be true across all ages, for both genders, and for all ethnic groups. It is not possible to ascertain whether effects of body composition on nonexercise activities occur independent of weight.

Limited data are available regarding differences in amount of physical activity performed during different seasons. Data from Canada suggest wide differences in time spent on physical activity due to season. Time spent on activity was twice as high during the summer months compared with winter months [59]. Common sense dictates and data confirm that occupational NEAT is greatly seasonally dependent in agricultural communities where workloads vary cyclically [60–62].

24 h energy expenditure

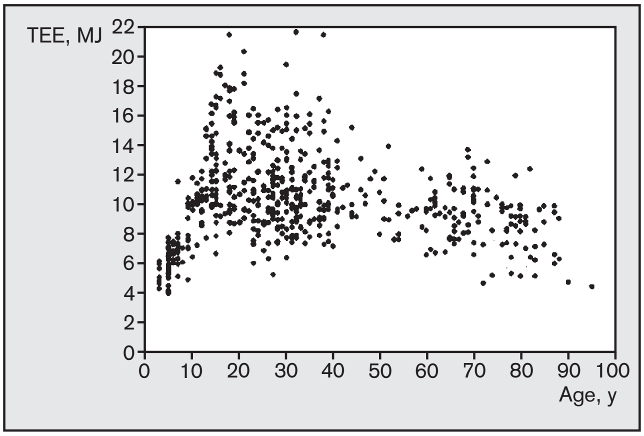
The CV for 24 h measurements of energy expenditure obtained using whole-room indirect calorimeters was 1–5% in weight-stable individuals [63–69]. We observed CVs of 4.6 ± 2.2% (range 1.5–8.2%) in 15 healthy, nonobese, weight-stable adults measured on four separate occasions (E.L. Melanson, W.T. Donahoo, W. Saris, unpublished data). However, room calorimeter studies tend to employ standard physical activity protocols, which limit spontaneous physical activity and possibly explain the low CV in 24 h energy expenditure. Although the CV for spontaneous physical activity in a room calorimeter is around 8–10% [66–68], the CV for 24 h energy expenditure is essentially unchanged after adjustment for day-to-day differences in spontaneous physical activity [68]. The CV in 24 h energy expenditure increases as the duration between measurements increases, rising from 2.7% when measured 1 day apart to 4.6% when measured 1–3 weeks apart [67]. The CV for RMR measured in a metabolic chamber is similar to that for RMR measured using the ventilated canopy technique [10–12,13••,14] but greater than the CV for 24 h energy expenditure [63,65,68]. However, the CV of sleeping metabolic rate tends to be similar to the CV for 24 h energy expenditure [63,68,69]. It has been suggested that the higher CVs during RMR may simply be due to the shorter duration of the measurements [63].

One study has considered the effects of menstrual cycle on 24 h energy expenditure. Webb [70] reported that 24 h energy expenditure was around 8% higher in the luteal compared with the follicular phase. Using the data presented in Table 2 in Webb's study [70], the average CV for 24 h energy expenditure was 2.1% in the follicular phase and 2.3% in the luteal phase. When values were averaged across the entire menstrual cycle, however, the CV for 24 h energy expenditure was 5.5%, which is similar to the CV in RMR across the menstrual cycle reported by Henry *et al.* [21•] (4.6%), but lower than that reported by Day *et al.* (11.1%).

Free-living energy expenditure

It is self evident that TDEE varies several-fold in humans. Black and colleagues [71] reviewed data from 574 measurements of TDEE and the key variables that predicted TDEE were body size, age, and gender (Fig. 1). The coarse relationship between TDEE and body size inevitably subjugates to physical laws. To this effect a small body (e.g. a mouse) loses more heat to its environment than a larger body (e.g. an elephant). However, the surface area to volume ratio and the laws of heat transfer for a homeotherm dictate that the energy expenditure per gram of weight is greater for a mouse than for an elephant. Similarly, the energy expenditure per gram of weight is greater for an infant than an adult. Thus with increasing size, TDEE increases in humans until they are fully grown (young adults). This not only reflects the thermodynamic consequence of increasing size, but the added thermodynamic inefficiency of growth. The thermodynamic inefficiencies that occur from birth through maturity are likely to impact RMR, DIT, and activity thermogenesis. Activity thermogenesis, corrected for body size, increases during this period. Although there are no longitudinal data sets or few cross-sectional analyses [71], the phenomenon of the high activity levels of unfettered children speaks of this ('mum, the kids are bouncing off the walls'). Thus, development through adulthood accounts for much of the variance in human TDEE overall.

Figure 1. Age for total daily energy expenditure (TEE) for 574 persons aged 2–95



Reproduced from [71].

Interestingly, once mature size is met, average TDEE starts to decline through middle age and continues to decline until death. This is likely to reflect several concurrent thermogenic mechanisms such as changes in body composition [72] and in physical activity. Another consistent factor that accounts for some of the variance in TDEE is gender. Women tend to have about 10% lower TDEE than men across the ages [56,71,73]; this effect is largely explained by differences in body composition, remembering that although lean tissue predominates energy expenditure, adipose tissue is thermogenic too [74]. Thus, core physical and biological processes predictably account for the coarse variance in TDEE that occurs across the ages.

The largest contributor to variance in TDEE is activity thermogenesis, and this variance might be explicable through the variance in exercise participation. Indeed, elite athletes have higher physical activity level values than the vast majority of developed-country dwellers [51,75]. Most Americans, however, take no regular exercise and even for those who do, NEAT accounts for the vast majority of activity thermogenesis and for the variance in activity thermogenesis. Hence, lifestyle and cultural milieu have been implicated as major predictors of activity thermogenesis, NEAT and its variability (Table 1). Impressively, these figures echo those derived from lower income societies [61,76] (Table 2).

Further insight into total activity thermogenesis comes from Westerterp's observation that in free-living individuals, the cumulative impact of low-intensity activities over prolonged duration is of greater energetic impact than short bursts of high-intensity physical activities [77]. Thus, for a given individual, their NEAT is defined by the sum of energetic cost of occupational plus non-occupational activities, which in turn is influenced by the sedentariness of the individual's microenvironment (e.g. workplace) and macroenvironment (e.g. country). What

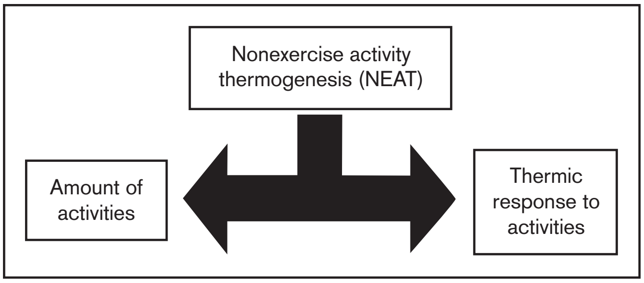
Table 1. Lifestyle-based prediction of physical activity level (PAL) values [71]

Lifestyle	PAL
Chair-bound or bed-bound	1.2
Seated work with no option of moving around and little or no strenuous leisure activity	1.4–1.5
Seated work with discretion and requirement to move around but little or no strenuous leisure activity	1.6–1.7
Standing work (e.g. housewife, shop assistant)	1.8–1.9
Strenuous work or highly active leisure	2.0–2.4

Table 2. Physical activity level (PAL) values of women and men from low-income countries, divided by intensity of work [61,76]

	Work intensity		
	Light	Moderate	Heavy
Women	1.55	1.64	1.82
Men	1.55	1.78	2.10

Figure 2. Components of nonexercise thermogenesis


Nonexercise activity thermogenesis (NEAT)
Amount of activities
Thermic response to activities

is fascinating is to speculate that a person with a high 'programmed NEAT' might select an active job (e.g. car washing or ambulatory mail delivery) despite living in a sedentary country such as the United States.

To systematically understand the variance in NEAT, we need to understand the variance in both the amount and energy efficiency of nonexercise activity. Since NEAT can be further divided into the amount of activities and the thermic response of these activities (Fig. 2), to understand the variance in NEAT requires an understanding of the variance of these two components. However, it is difficult to gain true estimates of free-living individuals' nonexercise activities because the variety of nonexercise activities is so enormous and the ability to quantify them so poor. What transpires from reviewing available data is, not surprisingly, that a variety of factors impact NEAT, including occupation, environment, education, genetics, age, gender, and body composition. Each of these factors will be discussed in the sections that follow.

The impact of occupation on nonexercise activity can be overt, for example when comparing the nonexercise activity of a laborer versus a civil servant [78–80]. Here, activity levels vary several-fold. There are more subtle occupational effects on physical activity. For example, in many populations where women work both in the home and out of the home, their cumulative work burden can exceed that of male cohabitants by several hours per day [56].

Groups with more education consistently report more leisure time physical activity than groups with less education. In the US, high education groups are two to three times more likely to be active than low education groups [51,53]. This contrasts with low-income countries, where child labor is commonplace. Here, poverty is predictive of greater child labor and the most impoverished children thereby have the greatest NEAT levels [56].

The importance of population sedentariness is well illustrated by studies of physical activity levels for individuals moving from agricultural communities to urban environments or of the effects of industrialization [81]. In many populations where this has occurred, urbanization has been associated with decreased physical activity. Sedentary cues are unmistakable in developed countries often through services designed to optimize convenience and throughput at the expense of necessitating locomotion. Examples include drive-through restaurants and banks, televisions, escalators, motorized walkways and clothes' washing machines. In the United States, schools may be built out of walking reach of the community served, suburbs built without pavements, city streets felt to be unsafe for leisure walking, or playgrounds unsafe for children to play in.

Genetics may play a role in determining the amount of nonexercise physical activity performed [82]. Based on twin and family studies, the heritability for physical activity level is estimated to be between 29 and 62%. Analysis of self-reports of physical activity from the Finnish Twin Registry, consisting of 1537 monozygotic and 3057 dizygotic twins, estimated a 62% heritability level for age-adjusted physical activity [83]. Analyses of self-reported physical activity from the Quebec Family Study, consisting of 1610 members of 375 families, showed a heritability level of 29% for habitual physical activity [84]. It is recognized that the boundaries between nonexercise and exercise-related energy expenditure may be poorly defined. Nonetheless, it is intriguing to speculate that genetics directly impact NEAT.

Conclusion

The difficulty in translating laboratory measurements of energy expenditure into long-term understanding of weight regulation is highlighted by the observation that there is substantial variation in energy intake [85], yet the average weight gain that has resulted in the current epidemic of obesity is of the order of 1 pound a year or approximately 10 kcal/day [86]. This small imbalance is less than 1% of RMR and TDEE, and is well below the limits of detection for many of the components of TDEE. It likely that NEAT contributes substantially to the inter and intrapersonal variability in energy expenditure. If three-quarters of the variance in basal metabolic rate can be accounted for by variance in lean body mass, and TEF represents 10–15% of total energy expenditure, then the majority of the variance in TDEE must be accounted for by variance in NEAT [87]. NEAT may play an important role in the physiology of body weight regulation. Indeed, changes in NEAT accounted for the differences in fat storage that occurred in response to experimental overfeeding [88], and evidence suggests that NEAT decreases during states of negative energy balance [87]. It is our opinion that future research should be directed at understanding how the components of NEAT contribute to the variance in TDEE.

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